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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,405	09/24/2004	Ilana (Helena) Nathan	P/4639-2	5690

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EXAMINER	
NIEBAUER, RONALD T	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
09/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,405	NATHAN ET AL.	
	Examiner	Art Unit	
	Ronald T. Niebauer	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *6-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *9/24/04* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to the contact information listed at the end of this action.

Election/Restrictions

Applicant's election of Group II (claim 2) and the species of elastase inhibitor III (MeOSuc-Ala-Ala-Pro-Val-CMK) for the elastase inhibitor; the regulation of expression by pro- and anti-apoptotic proteins for the inhibitor of apoptosis; neuronal cells as the cell type; dementia as the disease type in the reply filed on 6/19/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 6-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/19/07.

Claims 1 and 3-5 are linking claims and the species read on claims 1-5. Claims 1-5 are under consideration.

In the course of searching for the elected species other prior art to nonelected species was uncovered and is cited herein. It is noted that the claims have been examined with regard to the elected species, not the complete genus of species claimed. Compliance with, for example, 35

USC 112 1st paragraph (written description, enablement) and double patenting have only been considered with regard to the elected species and not to the complete genus of species claimed.

Specification/Drawings

The drawings are objected to because Figures 2-4 are indecipherable. Specifically, the background and foreground are not distinguishable and the protein bands such as those described in figure 4 (page 6) can not be seen. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,3-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and dependent claims 3-5 fail to interrelate essential elements of the invention since the claims do not recite an active step (see MPEP section 2172.01). Typically, a treatment includes an administration step.

Claim 3 refers to claim 1 and recites 'wherein the one or more agents administered...' There is insufficient antecedent basis for this limitation in the claim. Claim one does not recite any agents or administration of agents.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the treatment and prevention of dementia or the prevention of dementia. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As noted above, the claims have been examined with regard to the elected species, not the complete genus of species claimed.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

As noted above, the claims have been examined with regard to the elected species, not the complete genus of species claimed. The claims are drawn to a method of treating and/or preventing dementia.

Please note that the term "prevent" is an absolute definition which means to stop from occurring and, thus, requires a higher standard for enablement than does "therapeutic" or "treat", especially since it is notoriously well accepted in the medical art that the vast majority of afflictions/disorders suffered by mankind cannot be totally prevented with current therapies (other than certain vaccination regimes) – including preventing such disorders as Alzheimer's disease, which is clearly not recognized in the medical art as being a totally preventable condition.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The state of the art in preventing Alzheimers (a cause of dementia) is unpredictable.

As stated by Hingley (FDA document page 2):

"While researchers now have a deeper understanding of the brain and behavioral changes characterizing the disease, Alzheimer's remains shrouded in mystery. Its cause is still unknown...."
And (page 4)
"..no cure for Alzheimer's is available now..."

Further, Solomon (Expert Opin. Investig. Drugs 2007) discusses recent approaches for the treatment of Alzheimers (page 819). Solomon teach that (page 819) an increased knowledge of the pathophysiology of the disease and development of treatments and interventions are required for prevention of the disease (page 819).

(5) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

Examples (such as example 1) are provided in which model systems were used in vitro and cell death was monitored. However, the specification does not provide a correlation between the ability to treat a non-diseased population in vitro and the ability to treat a diseased population in vivo. Further, one of skill in the art would not accept that prevention of necrosis is the equivalent of the prevention of Alzheimers.

(8) The quantity of experimentation necessary:

Experimentation is required in numerous areas particularly related to how to use the method and determination if it would be a useful method for prevention of diseases. It is also unknown how much of an effect, if any, the method would have on disease states especially complex disease states such as Alzheimers. Considering the state of the art as discussed by the

references above, particularly with regards to the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Gyorkos et al. (US 6,001,813).

Gyorkos et al. teach a method of administering an elastase inhibitor to a host in need thereof (claim 10-11). Gyorkos teach that the inhibitors are useful for the treatment of conditions such as Alzheimer's disease (abstract and column 1).

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Miyano et al. (US 4,683,241).

Miyano et al. teach a method of administering an elastase inhibitor to a host in need thereof (claim 1) for the management of alleviation of elastase mediated diseases such as arthritis (column 1).

Regarding claim language, it is noted that section 2106 of the MPEP states:

> Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation.

In the instant claims, no active step is recited in claim 1. Language such as 'cause partial conversion...' (claim 3) does not limit the scope of the claim as it does not require steps to be performed. Further it is noted that the cells such as neuronal cells (claim 4) are present in the patient population of the above cited prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gyorkos et al. (US 6,001,813), and Stein et al. (Biochemistry 1986 v25 5414-5419).

Gyorkos et al. teach a method of administering an elastase inhibitor to a host in need thereof (claim 10-11). Gyorkos teach that the inhibitors are useful for the treatment of conditions such as Alzheimer's disease (abstract and column 1).

Gyorkos does not expressly teach the elected elastase inhibitor, elastase inhibitor III. Gyorkos teach tripeptides as inhibitors (claim 1 and abstract).

Stein et al. teach a chloromethyl ketone peptide (MeOSuc-Ala-Ala-Pro-Val-CH2Cl) as an elastase inhibitor (abstract) which is the elected species of the current invention.

Although Gyorkos does not expressly teach a specific embodiment of treating patients with Alzheimers, it would have been obvious to try the treatment on Alzheimers patients by identifying Azheimners from the known potential options listed in the abstract. A person of ordinary skill has good reason to pursue the known options within his or her technical grasp. Taken together, it would have been obvious to one of skill in the art to use the prior art elements taught by the references. One of skill in the art would have been motivated to substitute the chloromethyl ketone peptide disclosed by Stein for the tripeptide disclosed by Gyorkos because both are known elastase inhibitors. Since Stein teach that peptide derived chloromethyl ketones have desired qualities such as being irreversible inhibitors of serine proteases (elastase is a serine protease) one would be motivated to use these peptides in the method of Gyorkos. One would have had a reasonable expectation for success since the peptides used are known elastase inhibitors.

Regarding claim language, it is noted that section 2106 of the MPEP states:

> Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation.

In the instant claims, no active step is recited in claim 1. Language such as 'cause partial conversion...' (claim 3) does not limit the scope of the claim as it does not require steps to be

performed. Further it is noted that the cells such as neuronal cells (claim 4) are present in the patient population of the above cited prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ronald T. Niebauer whose telephone number is 571-270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rtn

8/29/07
ANISH GUPTA
PRIMARY EXAMINER